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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,858	05/22/2000	Richard O. Snyder	40447	2597

7590 01/28/2004  
STEVEN B. KELBER, ESQ.  
PIPER RUDNICK LLP  
1200 19TH STREET, N.W.  
WASHINGTON, DC 20036

EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT PAPER NUMBER

1632

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/576,858

**Applicant(s)**

SNYDER ET AL.

**Examiner**

Scott D. Priebe

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 November 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 92,94,96,98-101,105,106,109 and 115-119 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 92,94,96,98-101,105,106,109 and 115-119 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11/19/03 has been entered. Claims 92, 96, 100, and 109 have been amended. Claims 93, 95, 97, 102-104, 107-108, and 110-114 have been cancelled. Claims 115-119 have been added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection under 35 USC 102 over Srivastava is withdrawn in view of the amendment.

### ***Claim Rejections - 35 USC § 112***

Claims 92, 94, 96, 98-101, 105, 106, 109, and 115-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Claims 92, 94, 96, 98 and 99 recite that the AAV comprises a constitutive promoter, fIX coding sequence, and bovine growth hormone polyA sequence (bGH pA). Claim 96 limits the promoter to one of a MFG promoter, CMV promoter, or RSV promoter. Claims 100, 101, 105, 106, and 109 recite that the AAV comprises a MFG promoter, fIX coding sequence, and bovine growth hormone polyA sequence. Applicant points to pages 24-26, 31, 32, and Fig. 6 for support for claim 109, but fails to indicate where the specification supports the combination of the bGH pA with any constitutive promoter other than the promoter comprising an MFG promoter (MuLV 5'-ITR) linked to the adjacent MLV intervening sequence (MuLV IVS) and env ATG codon. The original specification discloses the use of the bGH pA only in conjunction with embodiments of AAV vector described in Fig. 6. The original specification does not mention, even in passing, broader AAV vectors, with respect to the promoter, where the bGH pA is included. Claim 96 recites the constitutive promoter can be the MFG promoter. The instant specification does not support AAV vectors which contain this promoter, but lack the adjacent MuLV IVS and env ATG sequence, as shown in Fig. 6.

Claim 96 recites that the constitutive promoter can be the CMV or RSV promoter. Applicant argues that the CMV and RSV promoters were well known constitutive promoters, and fails to indicate where the specification teaches using either of these promoters. Claims 115-119 are directed to embodiments where the promoter comprises the thyroid hormone-binding globulin promoter and two copies of the  $\alpha$ 1-microglobulin/bikunin enhancer. Applicant argues that the teaching in the specification of using a generic liver specific promoter supports this limitation. However, the specification fails to disclose this promoter. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when

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combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose.” *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

Claims 92, 94, 96, 98-101, 105, 106, 109 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 2/19/03 because the specification, while being enabling for embodiments wherein the rAAV consists of AAV terminal repeats flanking in order an MFG promoter ( Moloney murine leukemia virus 5' LTR), adjacent MLV intervening sequence including the splice donor and acceptor sites and env ATG, a Factor IX coding sequence, and bovine growth hormone polyA sequence (i.e. the construct shown in Fig. 6), and wherein the mammal has hemophilia B, does not reasonably provide enablement for other embodiments embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In addition to the formally stated reasons of rejection in the Office action of 2/19/03 from pages 3-9, the following reasons taken from the response to Applicant's arguments at pages 11-12 of the Office action are hereby incorporated into the rejection proper.

Koeberl discloses two different rAAV encoding fIX; one consists of AAV terminal repeats flanking in order the MLV promoter (but lacking the adjacent MLV IVS), fIX coding sequence, SV40 promoter, neo coding sequence and SV40 polyA sequence, and the second consists of AAV terminal repeats flanking an RSV promoter, fIX coding sequence and AAV polyA sequence. Administration of both rAAV to mice (C57BL/6J) resulted in similar, sub-

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therapeutic levels of fIX expression, even with irradiation and administration of wild type AAV to increase transfection efficiency. Snyder (1997) disclosed another rAAV that had a CMV promoter in place of the MFG promoter, MuLV IVS and env ATG, which also failed to yield therapeutic levels of fIX expression in mice. The MLV, RSV, and CMV promoters are all constitutive promoters routinely used in putative gene therapy vectors. Taking Koeberl, Snyder (1997) and the instant specification together shows three unsuccessful constructs and only one successful construct. Thus, there is and was considerable unpredictability as to which specific rAAV would be successful. There are no teachings in the instant specification to indicate that the specific construct would be important for achieving therapeutic levels of expression in mice or any other mammal, nor does applicant offer any explanation as to why the one example disclosed in the specification succeeded while other similar rAAV failed. This suggests that the specific elements of the rAAV are critical to success, contrary to the general teachings of the specification. Consequently, the instant specification does not generally enable using a generic rAAV which can express fIX in the context of the claims, but only the specific rAAV described by Fig. 6.

Applicant's arguments filed 11/19/03 have been fully considered but they are not persuasive. Applicant asserts that the specification taught one skilled in the art how to make and use the full scope of the claimed invention without undue experimentation, and argues that this assertion taken together with the amendments obviates the rejection. In response, Applicant has failed to address the substance of the rejection, and the amendments do not address the full extent of the rejection. As indicated in the amended rejection, several of the embodiments explicitly recited in the claims, e.g. use of RSV or CMV promoter, had been tried before or

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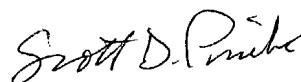
shortly after (by Koeberl et al. and Snyder et al. (1997) respectively) the instant application was filed, and failed. Likewise, embodiments where the MFG promoter alone, without the adjacent MuLV IVS and env ATG, had also been tried by Koeberl and had failed.

Further limiting claims 100, 101, 105, 106, and 109 to include the MuLV IVS and env ATG between the MFG promoter and flX coding sequence would obviate the rejection of these claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Scott D. Priebe  
Primary Examiner  
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